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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,278	06/29/2001	Gilbert Lavielle	ADIR360/Iw	7985

7590

11/25/2003

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EXAMINER

BERNHARDT, EMILY B

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 11/25/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/896,278

Applicant(s)

LAVIELLE ET AL.

Examiner

Emily Bernhardt

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 18-26,28(?),29 and 32-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 18-26,28,33 and 34 is/are rejected.
- 7) ☒ Claim(s) 29 and 32 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15. 6) ☐ Other: _____

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/8/03 has been entered.

Applicants have been advised that amendment filed 9/8/03 was not entered by the PTO staff because it did not conform to new Rules governing amendments. The supplemental amendment filed 9/16/03 has been entered. Status of claims require clarification. Claims 27,30 and 31 are indicated as "withdrawn" yet these claims were previously cancelled. "Withdrawn" and "cancelled" have quite different meanings and applicants are advised to carefully review all subsequent amendments to avoid confusion or non-entry. Also claim 28 is stated to be "withdrawn" yet was examined in previous actions and in current amendment is indicated as pending yet all the text has been deleted resulting in a par. Two rejection below.

Claims 18-26, 28 and 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Status of claim 28 is unclear as stated directly above. Is it really a cancelled claim?

2. "Containing" appearing at the end of main claim 18 in the alkyl and alkoxy definitions is open-ended and thus implies more than what is positively recited.

"Having" is suggested. Also note the typo "alkyl-oxy" appearing in the "alkoxy" definition.

Claims 33 and 34 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The uses other than those indicated as enabled in the previous action remain nonenabled for the following reasons notwithstanding the list of references provided in the 2nd Declaration by Dr. Millan filed on 9/8/03. The references for the most part are largely concerned with the elucidation of the possible mechanism of action for a particular disease rather than providing clinical evaluation for whole classes of disorders as claimed herein. With regard to refs. 1-20 listed under "Sexual dysfunction" (SD) and Libido disorders, the majority of these deal with yohimbine, a known alpha-2 adrenoreceptor antagonist, for treating male impotence – not any and all types of male and female sexual dysfunction- and for increasing male sexual arousal. Note Bitran abstract: "...no drug has been found to affect only a single component." . In Danjou it is stated on p.733: "In man studies on yohimbine have shown contradictory results regarding the effects of the drug on the sexual activity of impotent patients..." . In Susset on p.1363 it is stated: "The mechanism of the drug action remains unclear." . In Morales the most recent article cited on SD, note concluding remarks regarding clinical efficacy in

man on p.573. Refs. 15 and 16 deal with 2 other drugs having adrenergic antagonistic activity. These are considered likely candidates for treatment of male erectile dysfunction. In contrast applicants state in the specification on p.39 that their compounds "inhibit" penile erection- the opposite effect discussed in refs. 1-16 and thus it is not seen how these references support a class of disorders that read at the very least on diametric opposites. Refs. 17-20 while dealing with drugs acting on serotonin receptors discuss both stimulation and suppression of sexual performance depending on the type of receptor involved as discussed on p.1264 of Foreman (ref.17). 5-HT_{2c} receptor antagonists appear to be inhibitory consistent with applicants' statement in the specification .

The references (21-28) dealing with schizophrenia are similar to those previously provided by applicants since compounds being described as atypical antipsychotics are all dopamine active. Applicants have not addressed this point made previously by the examiner. Additionally, it is not clear if the 5-HT_{2c} receptor is responsible for the reduction of side effects since compounds such as clozapine interact with many neurotransmitter receptors as discussed on p.91-92 in Wood (ref.24). With regard to cognitive function (although cognitive disorders is recited in the claims), refs. 29-36 are no more persuasive than those previously provided. Idazoxan discussed in refs.29-31 is described as being a selective α_2 -

antagonist with very limited applications towards certain aspects of attention and memory . Even for these uses the results are preliminary as discussed in the concluding section of Coull on p.247. Atipamezole on the other hand , also an α_2 -antagonist did not facilitate attention processes as stated at the end of the Sirvio article (ref.34). Pascual (ref.32) while discussing a link to Alzheimer's Disease and quantity of α_2 -adrenoreceptors in the brains of AD patients concludes that α_2 -agonists would not improve the "catecholaminergic deficit of AD brain" . Refs. 35 and 36 deal with additional test results for other α_2 -antagonists. In Haapalinna (ref.35) note the contrasting results obtained for yohimbine vs. atipamezole as discussed on p.37 and 38. Chopin deals with dexefaroxin which is taught has potential in improving memory deficits based on its ability as a specific and competitive α_2 -antagonist. Thus these references at best deal with a small portion of what constitutes cognitive disorders, and with varying results based on the drug tested despite the common mode of action. Defects such as mental retardation, all forms of dementias (eg. Pick's Disease, multi-infarct, drug-induced), all types of learning disabilities (dyslexia, autism, etc.) and amnestic syndromes are all additional examples of what constitutes cognitive disorders for which no evidence of clinical efficacy is seen.

References (37-40) deal with only one particular type of sleep disorder, namely slow wave sleep (SWS) which is not particularly described by applicants nor shown would cover such sleep disorders as narcolepsy, sleep apnea, sleepwalking, insomnia all covered by the broader claim language. It is noted that none of the references address drug abuse another very broad class of diseases covered. In conclusion, the references neither individually nor collectively evidence the myriad of uses claimed as being art-recognized as being treatable in the serotonin/ alpha-adrenergic art in general much less based on the particular activities described for instant compounds. Note that composition claim 34 is also rejected since it recites the rejected uses as well.

Note the criteria for enablement as set out in *In re Wands* cited in MPEP 2164.01(a), August 2000 edition. Thus given the level of skill in this art which is low and the lack of direction (i.e. art-recognized tests) provided as to what might be treatable and in what dosage compounds are to be administered, this rejection is being applied.

Claims 29 and 32 remain objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Any inquiry concerning this communication should be directed to Emily Bernhardt at telephone number (703) 308-4714.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The new fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

E Bernhardt
EMILY BERNHARDT
PRIMARY EXAMINER
GROUP 1600